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10/031,081	01/16/2002	Osamu Terasaki	TAKIT 162	6139

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EXAMINER
SOUW, BERNARD E

ART UNIT	PAPER NUMBER
2881	

DATE MAILED: 05/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/031,081	TERASAKI ET AL.	
	Examiner	Art Unit	
	Bernard E Souw	2881	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03/11/2003 (Amendment A, paper no.7/a)* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *3/11/2003 (paper no.4)* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7/a* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *9* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Amendment

1. The Amendment A, filed on 03/11/2003, Paper No.7/a, in response to the first Office Action mailed October 24, 2002, has been entered.

Claims 1 and 6 have been amended,

New claims 7 and 8 have been added, and

The present Office Action is made with all the claims and suggested amendments being fully considered.

Substitute Specification

2. New substitute Specification, filed 03/11/2003, has been entered (paper no.5)

Formal Drawings

3. New formal drawings (Figures 1-4), filed 03/11/2003, have been entered (paper no. 4).

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on 03/11/2003 along with the Amendment A (paper no.7/a) was filed after the mailing date of the 1st Office Action on 10/24/2002. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Objections to Specifications

5. A new, substitute specification having been entered (paper no.5), the previous objections to the specification are now withdrawn, also including the TEXT FILE, which appears to be no different than conventional data file for computer data processing, and hence, should not have been given any special attention and/or distinguished value.

However, the lengthy new substitute specification has not been checked to the extent necessary to determine the presence of all possible errors. Applicant's cooperation is requested in correcting any error of which Applicant may become aware in the substitute specification. All errors should be corrected prior the application can be allowed.

Supplemental Information

6. Supplemental information regarding Applicant's invention has been received 05/01/2003 through Applicant's Attorney (paper no.8). However, the information thereby provided has failed to answer the Examiner's repeated request for specifically identifying the novelty of Applicant's invention as compared to the recited prior arts, specifically Dorset's (previously used as primary prior art in the § 102 rejections), Bendersky et al. (recited in the previous § 112 rejections), and other references already cited in previous PTO-892 (see previous Office Action, pg.6/lines 5-9), such as Baumeister et al. in Trends in Biochemical Sciences 25 (12), 2000, specifically as described on pp. 624-625, Col.3, section Electron crystallography, Box 1 & Fig.1 (new

citation). Instead of addressing Examiner's specific question regarding novelty, Applicant's lengthy explanation merely describes *what* Applicant's invention has done, but failing to answer the specific question, *how*, as required to distinguish Applicant's invention from the above cited references.

However, Applicant's referral to two publication articles has finally led to the conclusion that Applicant's method of determining the phases of the structure factors is no different than those employed in the above cited references.

Response to Applicant's Arguments

7. Applicant's arguments filed 03/11/2003 (paper no. 7/a) have been fully considered but they are not persuasive. The following is the Examiner's response to Applicant's arguments.

► Applicant's argument regarding the previous § 102 rejection is based on a misinterpretation of Examiner's ground of rejection, i.e., the "Direct Method", which – despite Examiner's clear identification with reference citations, is misinterpreted by Applicant as being a "Direct Method" as conventionally understood in X-ray (also electron) ***diffraction***, in which the phase information of the structure factors are lost, and has to be recovered by a method involving initial guessing and trial & error technique.

What was meant by Examiner was very clearly the 'Direct Method' not in term of X-ray diffraction, but its equivalent method in High Resolution Electron Microscopy (HREM), as defined by Dorset, pg 213, column 1, last paragraph, lines 1-2, already

recited in the previous Office Action, i.e., through Dorset's wording "*while the Fourier transform of an **electron micrograph** would be the most easily imagined '**direct method**' .. "*. The words *Fourier transform* (previous Office Action, pg.8, lines 7-10, reciting Dorset pg.212, col.2, lines 31-38 and pg.213, column1, lines 6-15 from bottom) and ***electron micrograph*** (previous Office Action, pg.8, lines 4-5) unambiguously expressed that what was meant by Examiner was not the Direct Method as conventionally known in X-ray crystallography, which is solely based on diffraction data and does not make use of electron micrograph data (= physical image ~ electron density $\rho(r)$).

Note: While the first citation regarding Fourier Transform (FT) was correct, the second citation "*pg.213, column 1, lines 21-24*", was a *misprint*, which should correctly read ***lines 53-55.*** Proof for this misprint is, those misprinted lines do not contain or match the phrase identified in the context, i.e., ***electron micrograph***, which is recited in lines 53-55.

Contrary to Applicant's argument, Dorset's FT of electron micrograph (=*most easily imagined 'direct method'*) yields crystallographic *phases after image analysis*, as unambiguously recited in the next immediate lines already recited above, i.e., Dorset pg.213, Col.1, lines 7-8 from bottom. In direct contradiction to Applicant's allegation (Applicant's paper no.7/a, pg.5, lines 7-9), there is neither "initial estimation" nor "*trial and error*" in deriving the phases from the FT of micrograph images according to Dorset, here used by the examiner to reject claim 1 under § 102.

Applicant's misinterpretation of examiner's ground of rejection is further revealed by previously cited *risc2.numis.edu* reference dated June 1999, downloaded from http://www.numis.nwu.edu/fs98, on pg.1 of 2, lines 1-11. Especially lines 5-6 recite "... *when you already have some phases from, for instance, a HREM image* ***and*** *transmission electron diffraction data*". As recited above, HREM is also known as *electron micrograph image*, as generally also known in the art. Thus, the "*numis*" reference (as also Dorset's) unambiguously identifies that crystallographic phases are obtained from the FT of HREM image ***plus*** the TEM data *directly*, *without guessing or trial & error method* as alleged by Applicant (paper no.7/a, pg.10). Note, the "*numis*" reference is not being used in the § 102 rejection, but is here cited just to show Applicant's misinterpretation of Examiner's citation of FT of HREM image as being the conventional Direct Method as known from the X-ray diffraction. However, the method of "*numis*" reference is inherent in Dorset's.

A further proof for Applicant's misinterpretation of this examiner's ground of rejection is further revealed by Kaneda et al., which recites on pg. 1256, col.2, lines 6-9, that "*HREM images can be taken and that the phases of crystal structure factors (CSFs) are immediately available from the Fourier transform (FT) of the (HREM) image*". Again, the Kaneda reference is here not being used by the Examiner as a prior art for rejecting Applicant's claims because Applicant is one of the authors (although he is not automatically a co-inventor of the method, unless an Affidavit can be provided, if this Application is to be allowed), but is merely being used to demonstrate that Applicant's method of Fourier transforming HREM images to obtain the phases, as described in

Kaneda reference, is no different than the well known method described by Dorset (applied as prior art) as well as in "*risc.numis.edu*". Therefore, Applicant's *invention* lacks novelty, for being well known in the art and also widely used prior to Applicant's invention.

► Applicant's argument regarding the previous § 103 rejections is based on Attacking the prior arts Anderson and/or Subbiah individually. In this regard, one cannot show nonobviousness by attacking references individually, where 35 U.S.C. 103(a) rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In the instant case, Anderson's was taken as secondary prior art to render obvious the use of Dorset's method on light materials including porous materials. Similarly, Subbiah's reference was cited to render obvious the use of Dorset's method on other types of molecules specifically recited in Applicant's claims. In all cases, Dorset as modified by Anderson or Subbiah does uniquely determine the structure as a logical solution from experimental analysis, the latter being based on Dorset's direct method version of Fourier transform of HREM images assisted by TEM data taken from various crystallographic direction, i.e., features that are inherent in Dorset's.

35 USC § 112 Claim Rejections Removed

8. The substitute specification having declared the TEXT file as an ordinary and conventional data file, the previous § 112, 1st paragraph rejection is now revoked.

Despite Applicant's non-responsive answer on the specific question regarding (the phases of) *diffraction waves* in the Fourier transform of electron microscopy images, comparisons with the reference of "*numis*" as further described by Baumeister et al. provides the necessary information that leads to the conclusion, that Applicant's method, as described in Kaneda et al., which recites on pg. 1256, col.2, lines 6-9, that "*HREM images can be taken and that the phases of crystal structure factors (CSFs) are immediately available from the Fourier transform (FT) of the (HREM) image*", is *not distinguished* from the two references cited previously, in particular, in the 1st paragraph of section I. Introduction, of "*numis*" reference, which is the same as the method used by Baumeister et al., as described on pg. 625, Box 1, upper right hand corner of Fig.1, reciting that the amplitudes are obtained from electron diffractogram, whereas phases are obtained from FT of image.

As already implicated in previous Office Action (page 6, lines 2-4), Applicant's method neither distinguished from L.A. Bendersky & F.W. Gayle in "*Convergent Beam Electron Diffraction (CBED)*", J. Res. Natl. Inst. Stand. Technol. ***106***, 2001, pp.997-1012., specifically on pg. 998, Col.2, referring to Fig.2. This FT of HREM method is well known in the art, as indicated in all cited references, specifically by the words "*most easily imagined ...*" (Dorset), and "*when you are already have some phases ...*", ("*numis*" reference), also in Kaneda et al. by the words "*immediately available ..*", and is essentially inherent in Dorset's, here used in the § 102 rejection.

With the above conclusion, the previous § 112 rejections, 1st and 2nd paragraphs, regarding the specific method, how Applicant would determine the phases, and whether

or not Applicant's method is different or distinguished from the conventional method well known in the art, as described in Dorset's, Baumeister et al. and "*numis*", is now revoked, since answers to those specific questions have been found. This conclusion is made on the assumption that Applicant's claimed invention uses the same method as used in Kaneda et al., which is provided by the Applicant. In the event that Applicant would deny this assumption, Applicant is obligated to disclose the specific difference of Applicant's invention to the method of Kaneda et al. that would distinguish Applicant's invention from the well known method used in the cited references, as already repeatedly requested by the Examiner,

9. For reasons stated above, all the previous § 102 and § 103 rejections are here confirmed. They are repeated below, mostly in its original version without any change, except for some additionals (underlined) specifically addressing Applicant's arguments, including Applicant's amendment & addition of new claims 7 & 8.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2 and 7 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Dorset (Trends in Polymer Sciences Vo.4, No.7, July 1996, pp. 212-216).

Dorset discloses a method of determining a soft material structure (Dorset's polymer is a soft material per Applicant's definition of the terminology) by taking TEM images of the soft material under a plurality of crystallographically significant directions, as recited on pg.213/Col.1/ll.53-55 (former lines 21-24 was a misprint), which is inclusive in lines 6-15 from bottom recited previously. This method, which does not include "guessing" or "trial & error", and is to be clearly distinguished from the older form of direct method conventionally known in X-ray crystallography, but is mainly based on the Fourier transform of HREM images complemented by TEM diffraction data, is no different than the well known method as described in the "numis" reference, by Bendersky et al., and by Baumeister et al., as recited above.

Dorset's method sets forth with the step of Fourier transforming each of the ***images*** (HREM) photographed and evaluating therefrom amplitudes and phases of the three-dimensional crystal structure factors, as recited on pg.212/Co.2/ll.31-38 and pg.213/Col.1/ll.15-1 from bottom.

Dorset's method is accomplished by a further step of performing inverse Fourier transforms by use of the values evaluated, as recited on pg.212/Col.2/ll.20-12 from bottom and on pg.214/Col.1/ll.11-14.

In the event Applicant would persist to argue that his method is distinguished from the cited prior art(s), and/or that the references fail to show certain features of applicant's invention, it is emphasized that the features upon which applicant relies is not found in the entire disclosure, nor is it recited in the claims. Even if they were hidden somewhere in the specification, limitations from the specification are not read

into the claims, although the claims are interpreted in light of the specification. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

- Regarding claim 2, Dorset's method includes the step of taking the ***TEM image*** of more than at least three different directions, as recited on page 213, col.1, 2nd paragraph, wherein three images is the minimum number in order to derive the 3-dimensional space group of the soft material sample, as generally known in the art.

This complementary method to Fourier transform of HREM image is inherent in Dorset's. Proof for such inherency has been meticulously detailed in the previous sections, whereas the necessity to rely on thin samples in order to avoid multiple scattering, as recited in Applicant's specification (pg.5, 2nd paragraph), is also recited by Dorset on pg.213, column 1, 3rd paragraph.

Regarding new claim 7, the limitation of Fourier transform of high resolution electron microscopy image (HREM) is already inherent in Dorset's, as specifically recited on pg.212/ll.31-38 (see previous rejections of claims 1 and 2).

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dorset in view of Anderson (US 2002/0102674 A1).

Dorset shows all the limitations of claim 3, as previously applied to claim 1, except the recitation of specific forms of soft materials, which is rendered obvious by Anderson.

Anderson's soft material is a porous material, as expressly recited as such in the Abstract/lines 1-5. Furthermore, Dorset's polymer belongs to light materials due to the hydrogen and carbon forming its major constituents, as generally known in the art.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to apply Dorset's electron crystallography method for determining the crystallographic structure of Anderson's soft/porous materials, thereby extending the classification of soft materials to include Anderson's porous materials such as biological membranes, since these molecules, too, are made of light atoms and have a periodicity of a substantial multiple of atomic sizes, i.e., in the range of 20-500 Å, in agreement with Applicant's private definition of the terminology, as generally known in the art.

13. Claims 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dorset's as modified by Anderson's, as applied to claims 1 and 3 above, and further in view of Subbiah (US 2002/0102674 A1, hereafter addressed by Subbiah-456).

Dorset's as modified by Anderson's shows all the limitations of claims 4-6, as previously applied to claim 1, except the recitation of a particular selection of specific materials as soft material, which is here rendered obvious by Subbiah-456.

Regarding claims 4 and 5, Subbiah-456's soft material matches Applicant's definition of the terminology. Subbiah's material is made of macromolecules, as recited in Col.1/ll.23-27 and Col.2/ll.33-39. In addition, Anderson's soft materials also include membrane polymers, as recited on pg.10/Col.2/section [0110].

- Regarding claim 6, Subbiah's macromolecules have periodicities up to 45 Å, as recited in Col.21/ll.15-20.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to extend the classification of soft materials according to Dorset as modified by Anderson, to include macromolecules and biological membranes, as specified by Subbiah, since these molecules, too, are made of light atoms and have a periodicity of a substantial multiple of atomic sizes, i.e., in the range of 20-500 Å, as generally known in the art.

14. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dorset in view of Koshishiba et al. (USPAT # 5,051,585) and Coene (USPAT # 5,432,347).

Dorset shows all the limitations of claim 8, as previously applied to claim 1, except the recitation that the influence of aberration in an objective lens for diffracted waves in a region of high spatial frequency is reduced through estimation of the amount of defocus using a ***Wiener*** filter (not *Weiner* filter).

Koshishiba et al. describe a pattern detection based on transmission electron micrograph, as recited in the Abstract. Koshishiba et al. teach that objective lens aberration may cause image deterioration in the form of resolution degradation, as

recited in Col.12/ll.25-29. It is generally known in the art of image processing (see Coene's teaching below), that image enhancement and/or restoration is conventionally achieved by enhancing the high frequency components of the Fourier transform, which inevitably would also increase the noise. Koshishiba further teach to use a Wien(er) filter in order to prevent noise enhancement, as recited in Col.6/ll.4-6.

Further, Coene describes a method for image reconstruction of HREM images, as recited in the Abstract and in columns 5-10. Coene also teaches to use Wien filter, as recited in Col.8/ll.48-52.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify Dorset's method of image processing by applying Wien filter as taught by Koshishiba et al. and Coene, since Wien filtering is a popular method in image processing to enhance high frequency features that are lost due to resolution degradation, such as caused by objective lens aberration, as specifically indicated by Koshishiba et al. in Col.12/ll.25-29.

One would have been motivated to apply a Wien filter especially for high resolution HREM images, since this filter is just appropriate for enhancing the resolution which contains high frequency components without enhancing the noise, as taught by Koshishiba et al. in Col.6/ll.4-6 and also by Coene in Col.8/ll.49-50.

15. Besides the previously applied rejection under 35 U.S.C. § 102(b), claims 1, 2 and 7 are ***additionally*** rejected under 35 U.S.C. § 103(a) as being unpatentable over Dorset.

Although Dorset does not expressly recite one or two steps in the limitations of claims 1, 2 and 7, these particular steps are inherent in Dorset (taken as Official Notice by the Examiner). The reason why Dorset does not expressly recite those few particular steps is just because they are very well known and have been being widely used in the art, as exampled in the "numis" reference, by Bendersky et al. and by Baumeister et al., as already described in the previous sections, as well as by many other authors that are needless to be further named in this Office Action because of their great abundance.

Final Rejection

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office Action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bernard E Souw whose telephone number is 703 305 0149. The examiner can normally be reached on Monday thru Friday, 9:00 am to 5:00 pm..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John R Lee can be reached on 703 308 4116. The fax phone numbers for the organization where this application or proceeding is assigned are 703 872 9318 for regular communications and 703 872 9319 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 0956.

bes
May 3, 2003

JOHN R. LEE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 2800